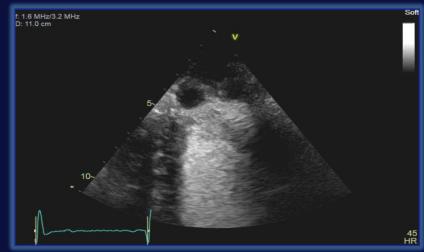
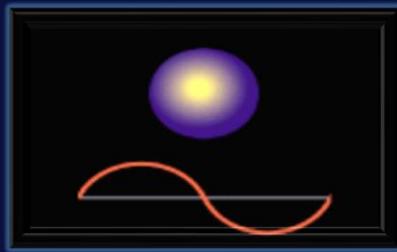


Contrast Echocardiography



Steven J. Lester, MD, FACC, FRCP(C), FASE
Mayo Clinic

DISCLOSURE

Relevant Financial Relationship(s)

None

Off Label Usage
Perfusion

Computerized Tomography



Magnetic Resonance



GUIDELINES AND STANDARDS

Clinical Applications of Ultrasonic Enhancing Agents in Echocardiography: 2018 American Society of Echocardiography Guidelines Update



Thomas R. Porter, MD, FASE (Chair), Sharon L. Mulvagh, MD, FASE (Co-Chair),
Sahar S. Abdelmoneim, MBBCH, MSc, MS, FASE, Harald Becher, MD, PhD,
J. Todd Belcik, BS, ACS, RDCS, FASE, Michelle Bierig, MPH, ACS, RDCS, FASE,
Jonathan Choy, MD, MBA, FASE, Nicola Gaibazzi, MD, PhD, Linda D. Gillam, MD, MPH, FASE,
Rajesh Janardhanan, MD, MRCP, FASE, Shelby Kutty, MD, PhD, MHCM, FASE,
Howard Leong-Poi, MD, FASE, Jonathan R. Lindner, MD, FASE, Michael L. Main, MD, FASE,
Wilson Mathias, Jr., MD, Margaret M. Park, BS, ACS, RDCS, RVT, FASE, Roxy Senior, MD, DM,
and Flordeliza Villanueva, MD, Omaha, Nebraska; Rochester, Minnesota; Edmonton, Alberta, Canada; Portland,
Oregon; Fort Myers, Florida; Parma, Italy; Morristown, New Jersey; Tucson, Arizona; Toronto, Ontario, Canada;
Kansas City, Missouri; São Paulo, Brazil; Cleveland, Ohio; London, United Kingdom; and Pittsburgh, Pennsylvania

This document is endorsed by the following American Society of Echocardiography International Alliance Partners: the Argentinian Federation of Cardiology, the British Society of Echocardiography, the Canadian Society of Echocardiography, the Chinese Society of Echocardiography, the Echocardiography Section of the Cuban Society of Cardiology, the Indian Academy of Echocardiography, the Indian Association of Cardiovascular Thoracic Anaesthesiologists, the Iranian Society of Echocardiography, the Japanese Society of Echocardiography, the Korean Society of Echocardiography, the Saudi Arabian Society of Echocardiography, and the Vietnamese Society of Echocardiography.

Keywords: Echocardiography, Contrast, Guidelines, Imaging

Objectives

- 1. Define ultrasound contrast?**
- 2. Recognize the interaction of the bubbles with ultrasound**
- 3. Describe how contrast maximizes value**
 - Incremental value for LVO
 - Incremental value for spectral Doppler
 - Structural abnormalities
 - Tissue characterization
 - Differentiate “real from Memorex”: Artifacts
- 4. Explain how to set up the pictures/pitfalls**
- 5. Perfusion**
- 6. Safety**

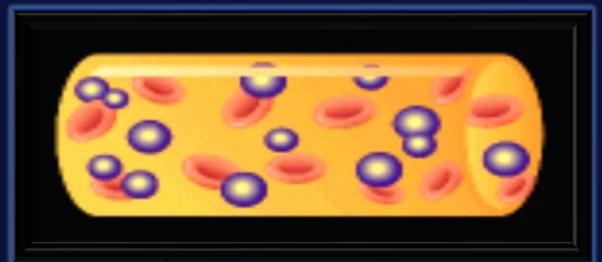
History

- Contrast enhancement with agitated saline solution or other fluids containing gas have been recognized for over 40 years.
- Bubbles of room air were either too big or dissolved too rapidly
- Therefore early contrast echocardiography was limited to shunt detection or the evaluation of right sided structures.

Cheng SC et al. *Am J Cardiol.* 1998;81:41G–48G.

Contemporary Ultrasound Contrast Agents

Stabilized gas microbubbles sized to pass through the smallest capillaries



FDA Approved Contrast Agents



Agent	Size (μm)	Gas	Shell	Indication
Optison	3.0-4.5	Perflutren	Albumin	LVO/EBD
Definity	1.3-3.3	Perflutren	Phospholipid	LVO/EBD
Lumason	1.5-2.5	Sulfur hexafluoride	Phospholipid	<ul style="list-style-type: none">LVO/EBDAbdominal/Liver USUrinary Tract (peds)

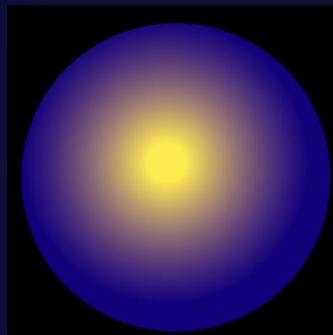
Bubble Characteristics



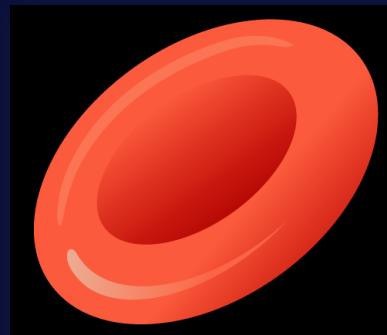
- Size
- Shell
- Gas

DeMaria. *Clin Cardiol.* 1997;20(suppl I):I-3.

Microbubbles - Size



Microbubble
1.5–4.5 μm



RBC
6–8 μm

Cheng et al. *Am J Cardiol.* 1998;81:41G.

Microbubbles - Shell

Shell Composition

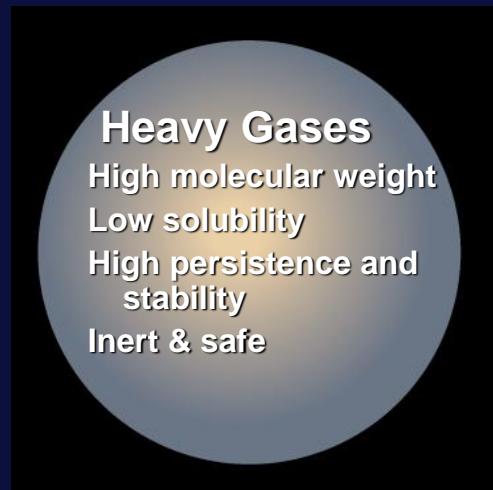
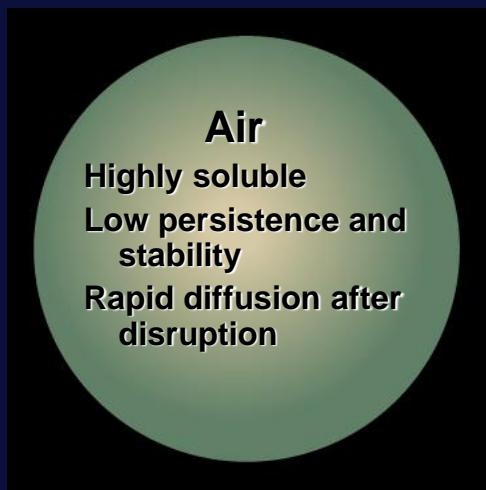
- Proteins
- Biocompatible polymers
- Phospholipids

Shell Properties

- Elasticity
- Fragility
- Biodistribution
- Elimination

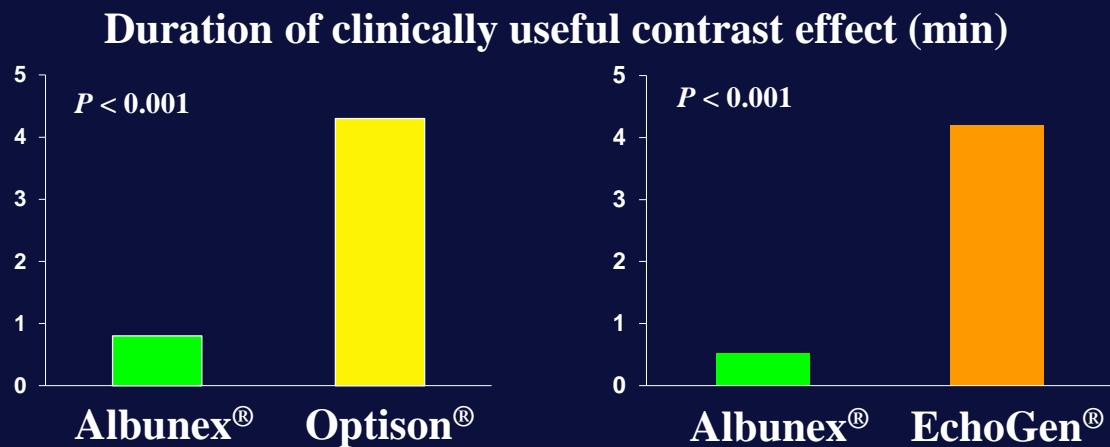
Burns PN. In: Rumack CM et al, eds. *Diagnostic Ultrasound*. Vol. 1. 2nd ed. St. Louis, MO: Mosby; 1998:57.

Microbubbles - Gas



Villarraga et al. *Tex Heart Inst J*. 1996;23:90.

Persistence: HMWG-Based Agents vs Albunex®



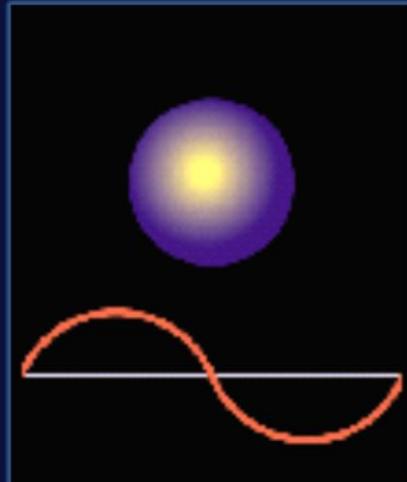
Adapted from Cohen et al. *J Am Coll Cardiol.*
1998;32:746.

Adapted from Grayburn et al. *J Am Coll Cardiol.*
1998;32:230.

Bubble Behavior in an Ultrasound Field

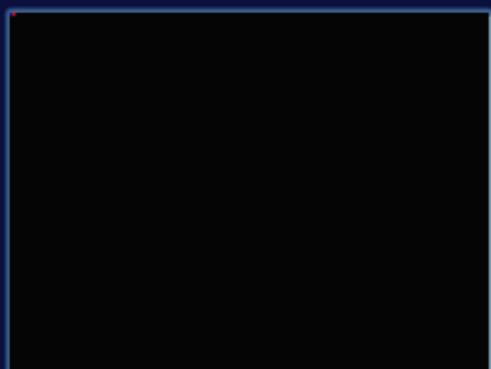
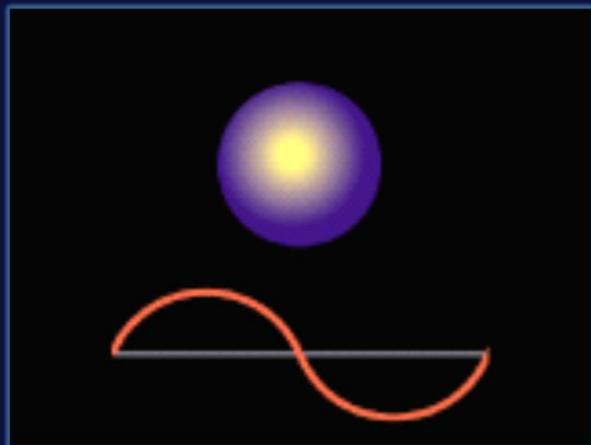
MI	Bubble Behavior	Acoustic Behavior	Clinical Application
< 0.1	Linear Oscillation	Backscatter Enhancement	Fundamental LVO Spectral Doppler
0.1-1.0	Nonlinear Oscillation	Harmonic Backscatter	Harmonic LVO Real time perfusion
>1.0	Disruption	Transient Harmonic Echos	Doppler LVO Triggered perfusion

Response of Bubbles to Ultrasound: Linear Resonance

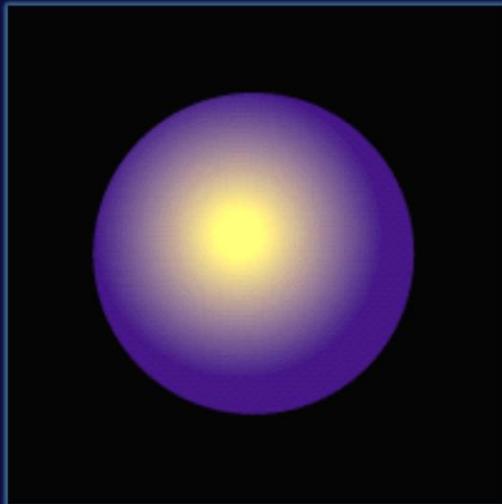


P. Burns & H. Becher. *Handbook of Contrast Echocardiography: LV Function and Myocardial Perfusion*. Springer; 2000.

Response of Bubbles to Ultrasound: Nonlinear Resonance



Response of Bubbles to Ultrasound: Transient Scattering

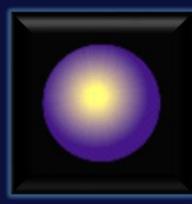


**Very strong
nonlinear
backscatter of
extremely short
duration**

Wei et al. *J Am Coll Cardiol.* 1997;29:1081.

Response of bubbles to Ultrasound

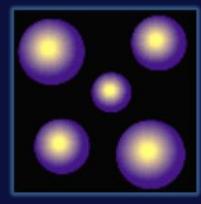
Linear resonance



Nonlinear resonance



Transient scattering



POWER

Fundamental enhancement

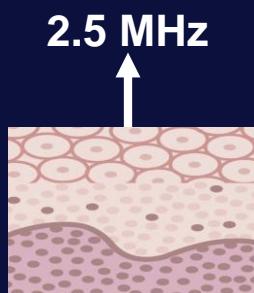
Harmonic enhancement

Bubble disruption

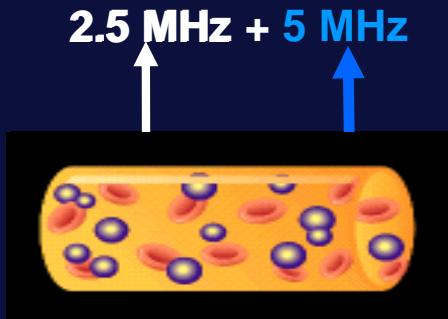
Burns PN. *Echocardiography.* 2002;19:241–258.

Principles of Harmonic Imaging

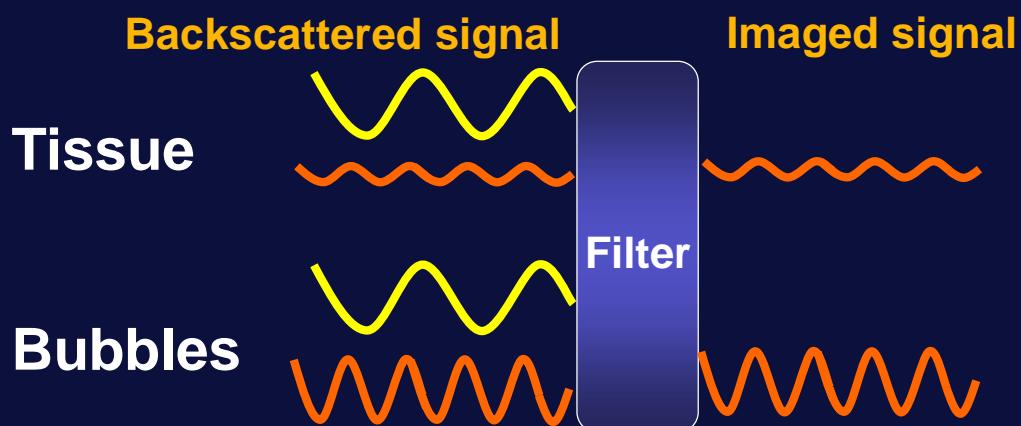
- Tissue and blood reflect at the fundamental frequency



- Microbubbles reflect at both the fundamental and the harmonic frequencies



Harmonic Imaging: Signal Filtering



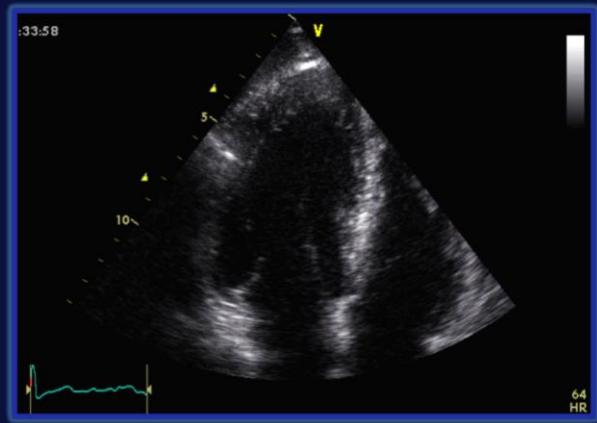
Burns. In Rumack et al, eds. *Diagnostic Ultrasound*. Vol. 1. 2nd ed. St. Louis: Mosby; 1998:57.

Objectives

1. Define ultrasound contrast?
2. Recognize the interaction of the bubbles with ultrasound
3. Describe how contrast maximizes value
 - Incremental value for LVO
 - Incremental value for spectral Doppler
 - Structural abnormalities
 - Tissue characterization
 - Differentiate “real from Memorex”: Artifacts
4. Explain how to set up the pictures/pitfalls
5. Perfusion
6. Safety

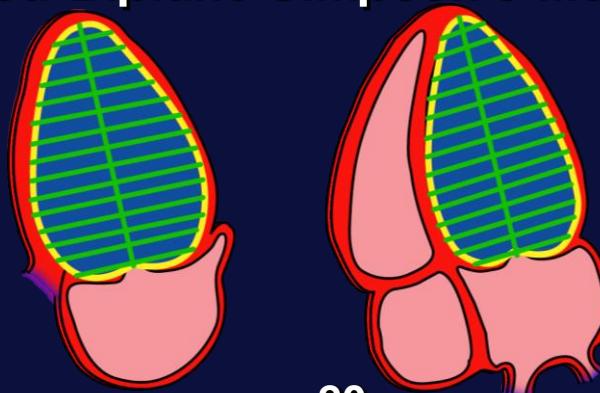
Echocardiography and Left Ventricular Function

- Most common use of diagnostic echocardiography
- Global ventricular function
- Regional wall motion
Rest
Stress



Left Ventricular Volume

Modified Biplane Simpson's Method

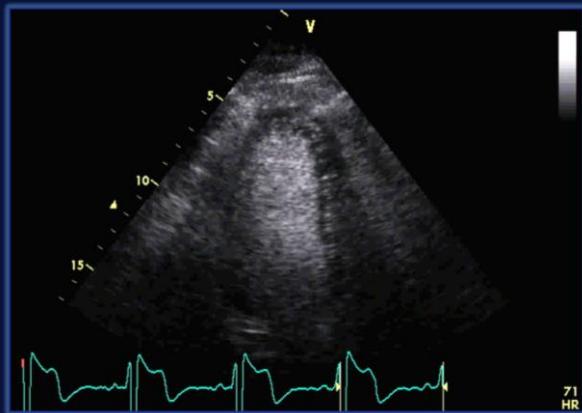


$$\text{Biplane volume} = \frac{\pi}{4} \sum_{i=1}^{20} a_i b_i \cdot \frac{L}{20}$$



Contrast Echocardiography

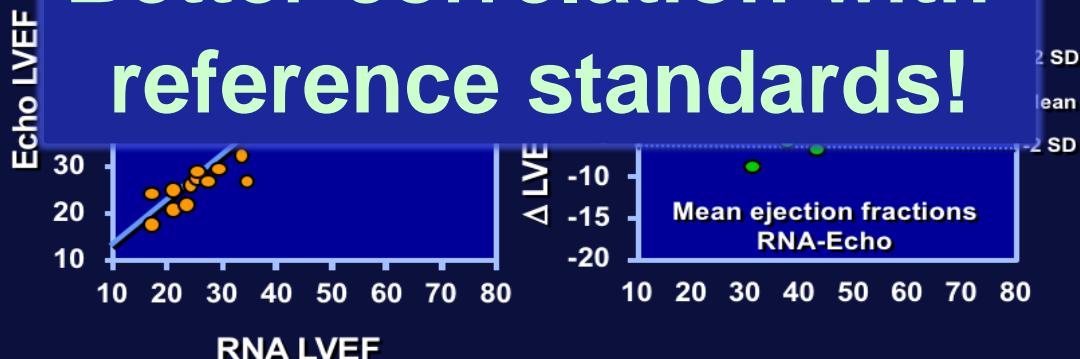
- Increased sensitivity
- Heightened diagnostic confidence
- Improved accuracy and reproducibility
- Enhanced clinical utility



LV Ejection Fraction

Echo Modified Biplane Simpson's Method vs. RNA Harmonic Imaging with Contrast

Better correlation with reference standards!

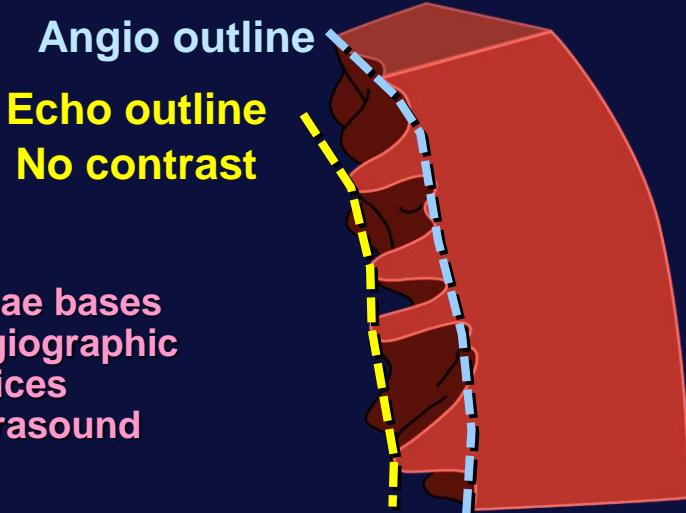


Nahar T et al: Am J Cardiol 86:1358, 2000

Left Ventricular Volume by 2-D Echo

Myocardial Border Detection vs Angiography

**Columnae carnae bases
enclosed by angiographic
dye vs apices
imaged by ultrasound**



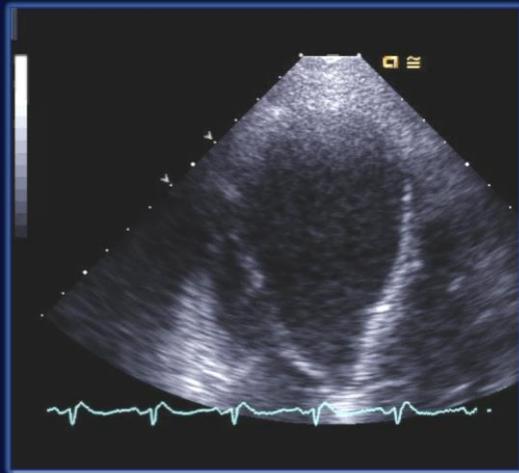
Schnittger I et al: Am J Cardiol 50:512, 1982

Contrast For LVO

Take Home Points

- 1. Defines the endocardial border better than unenhanced echocardiography.**
- 2. The underestimation of cardiac volumes by echocardiography is nearly resolved when contrast agents are used.**
- 3. Reduced intra and interobserver variability in measures of LV volumes and EF with better correlation with reference standards.**
- 4. Recommended for use when ≥ 2 LV segments are not well visualized.**

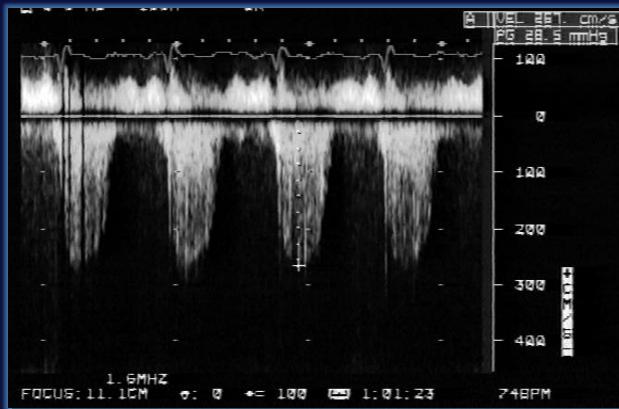
Why settle for this?



**When you can
have this!**



Incremental Value Spectral Doppler

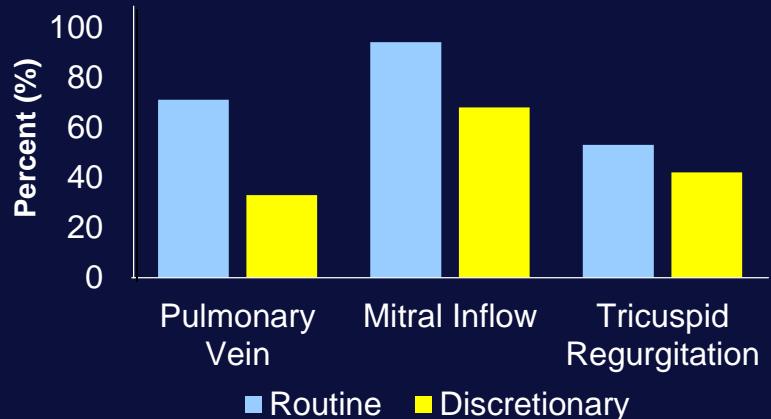


Spectral Doppler

Spectral Doppler

1= Excellent
2= Fair
3= Poor

Spectral Doppler Score = 1



Lester SJ et al. J Am Soc Echocardiogr 2006 Jul; 19(7):919-23

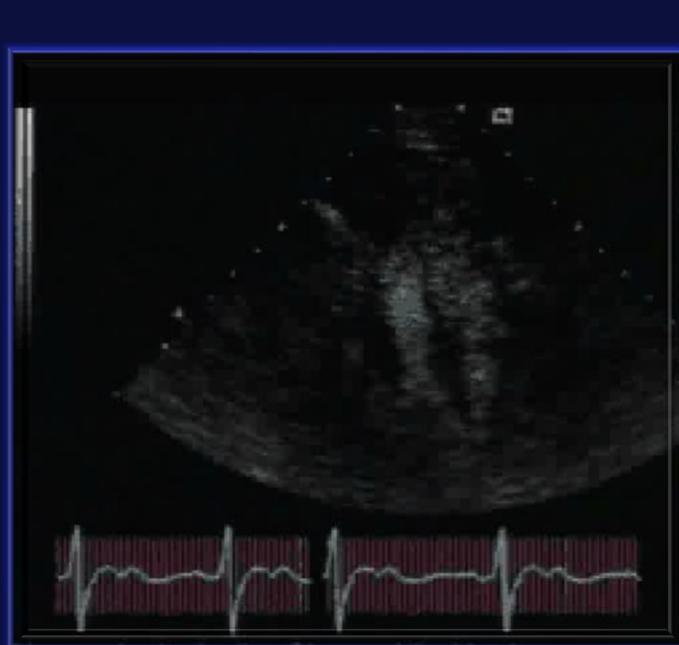
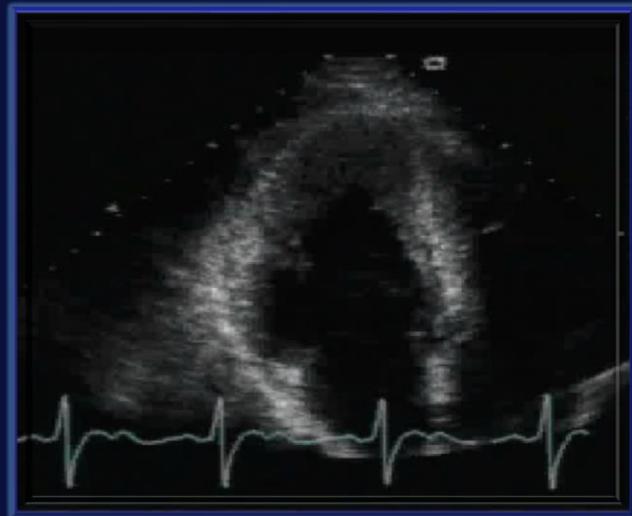
Contrast Echocardiography

Structural Definition

1. LV Structural Abnormalities

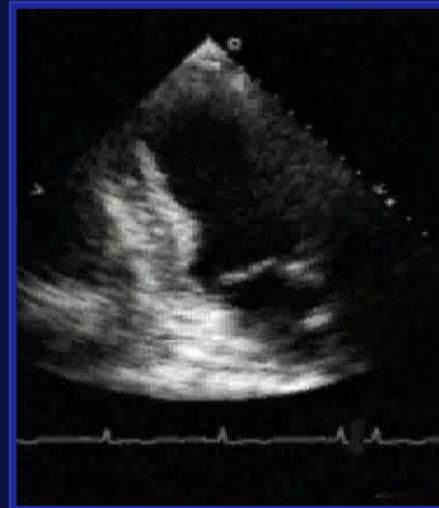
- Apical hypertrophy
- Aneurysm / pseudoaneurysm
- Thrombus
- Noncompaction
- Myocardial rupture

What's Up At The Apex?



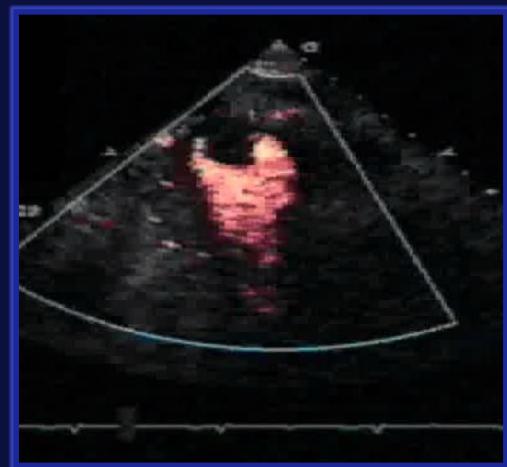
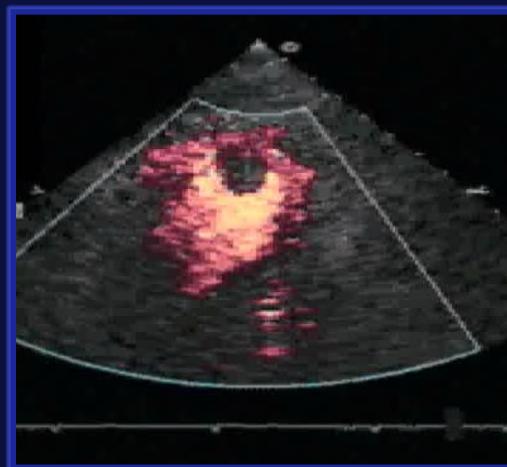
LV Structural Abnormalities

LV Aneurysm



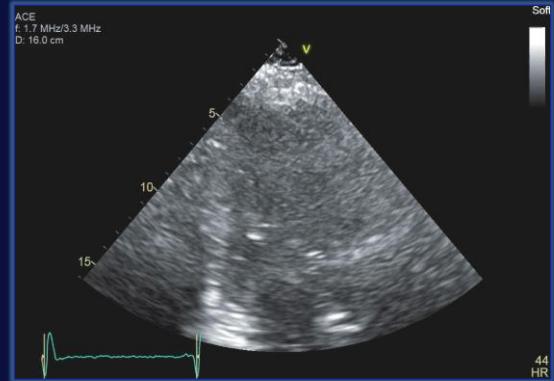
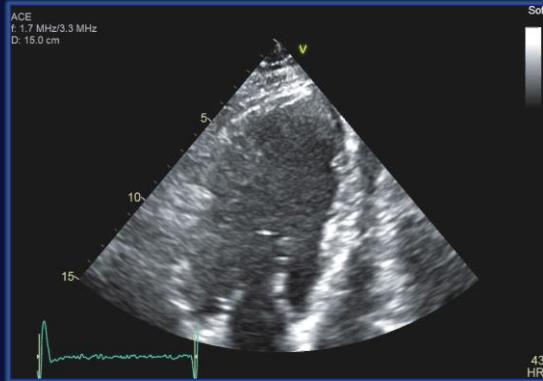
LV Structural Abnormalities

LV Aneurysm & More



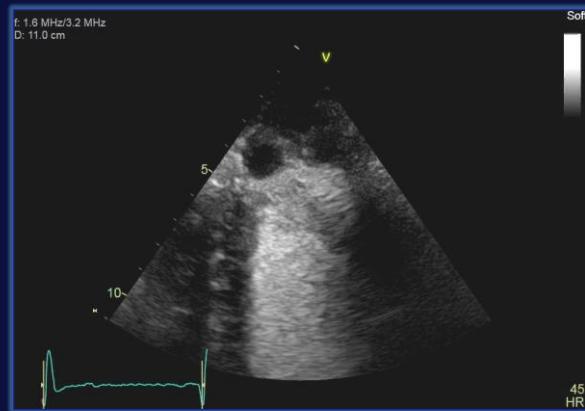
LV Structural Abnormalities

LV Aneurysm



LV Structural Abnormalities

LV Aneurysm & More



Contrast Echocardiography

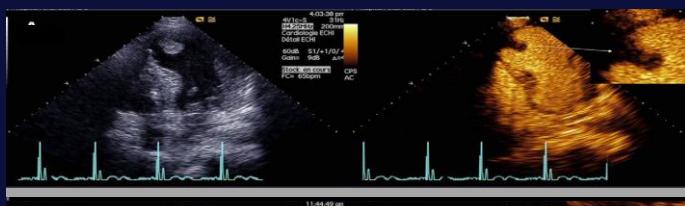
Structural Definition

1. LV Structural Abnormalities

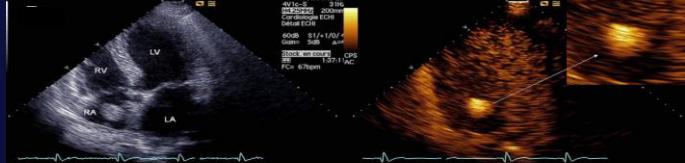
- Apical hypertrophy
- Aneurysm / pseudoaneurysm
- False chord
- Trabeculation: Noncompaction
- Myocardial rupture

2. Characterize intracardiac masses (tissue characterization)

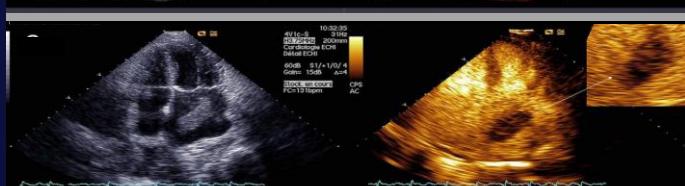
Characterize Intracardiac Masses



LV apical thrombus in patient post MI, no enhancement



Secondary cardiac tumor (renal sarcoma) located in RA, complete enhancement



LA myxoma, partial enhancement

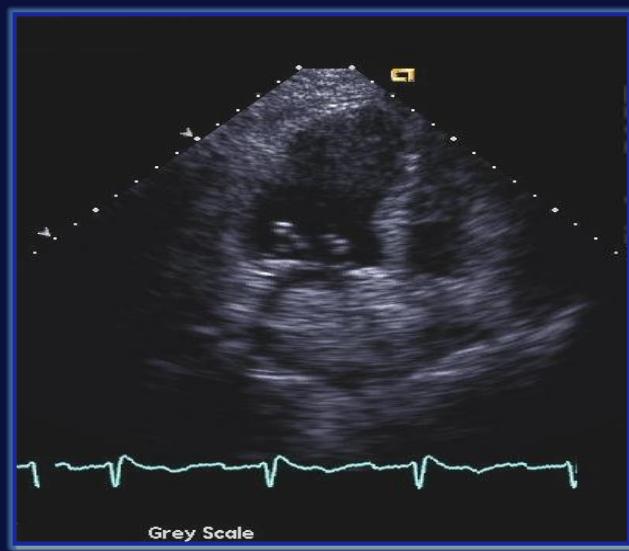
Mansencal et al. Archives of Cardiovascular Disease
(2009) 102, 177–183

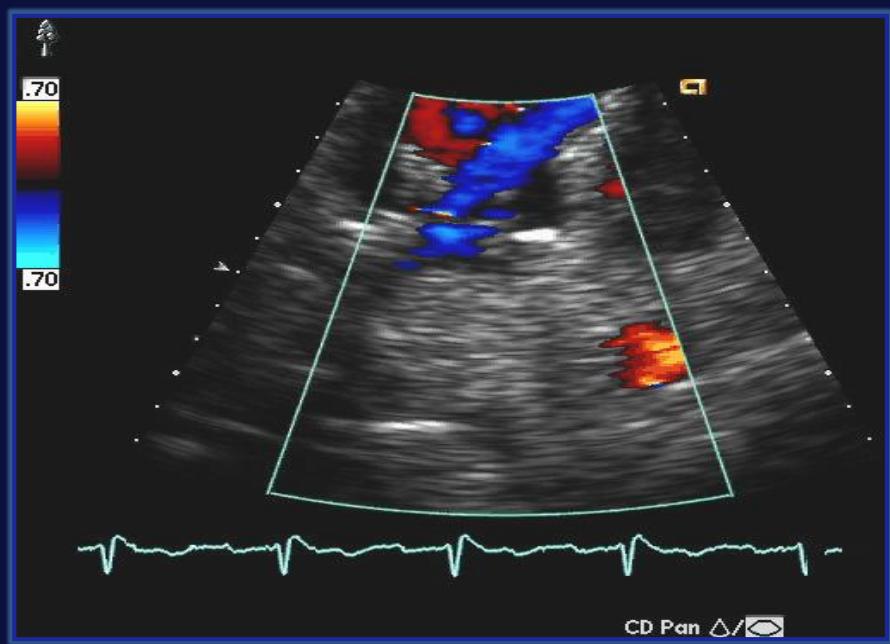
Contrast Echocardiography

Structural Definition

- 1. LV Structural Abnormalities**
 - Apical hypertrophy
 - Aneurysm / pseudoaneurysm
 - False chord
 - Trabeculation:Noncompaction
 - Myocardial rupture
- 2. Characterize intracardiac masses
(tissue characterization)**
- 3. Is it real or Memorex? Artifacts**

Left Atrial Myxoma?



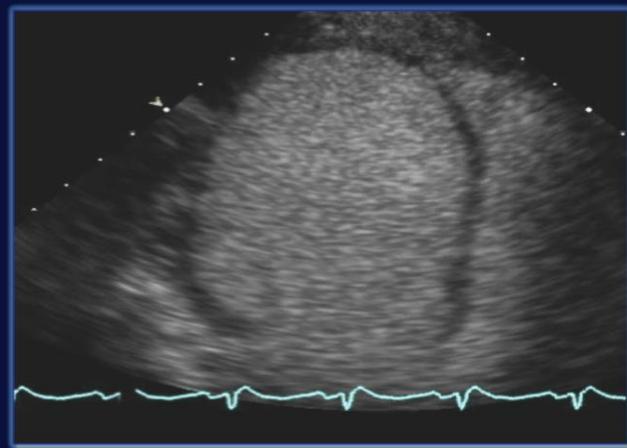


Objectives

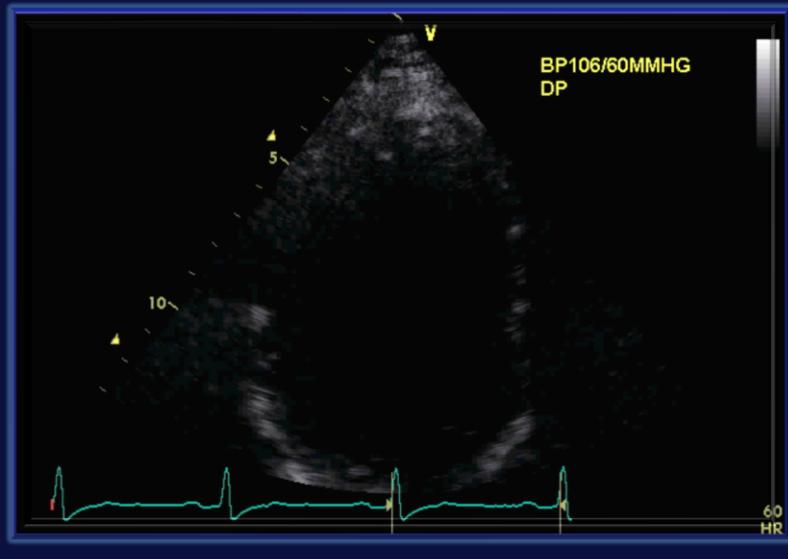
1. Define ultrasound contrast?
2. Recognize the interaction of the bubbles with ultrasound
3. Describe how contrast maximizes value
 - Incremental value for LVO
 - Incremental value for spectral Doppler
 - Structural abnormalities
 - Tissue characterization
 - Differentiate “real from Memorex”: Artifacts
4. Explain how to set up the pictures/pitfalls
5. Perfusion
6. Safety

Set Up and System Settings

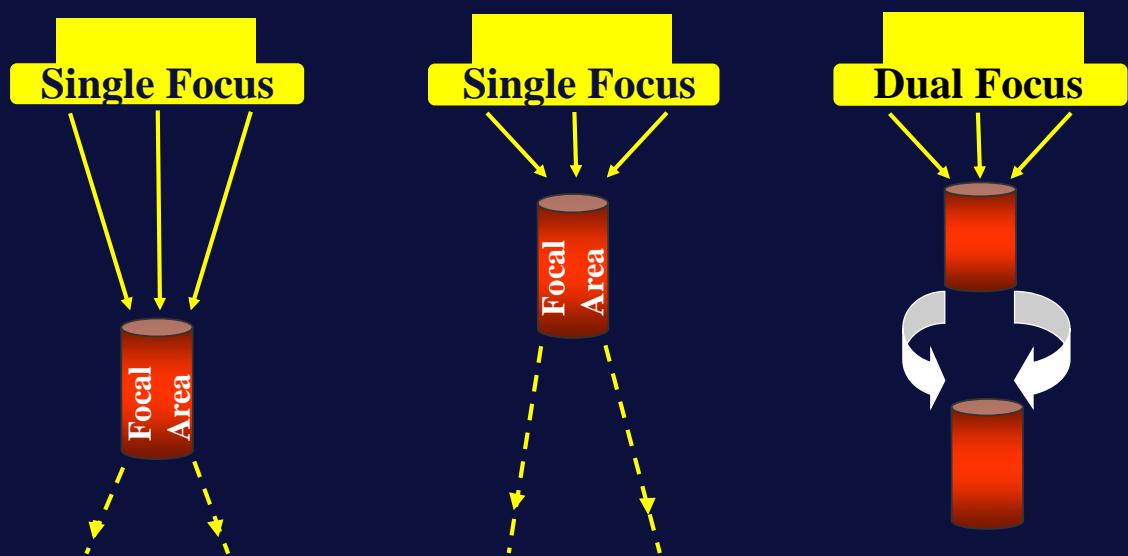
Machine and administration frequency adjusted
to provide the best image



Initial Image



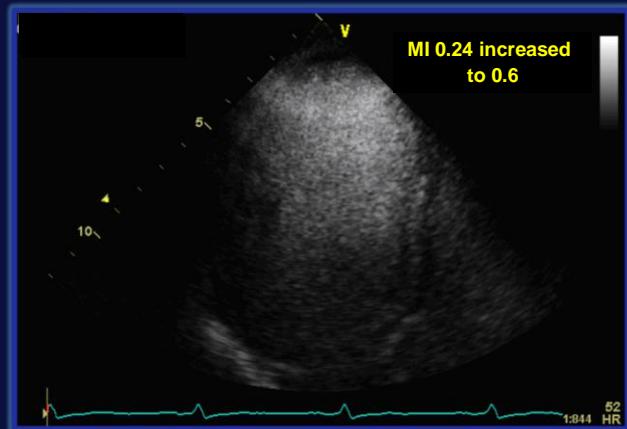
Focus



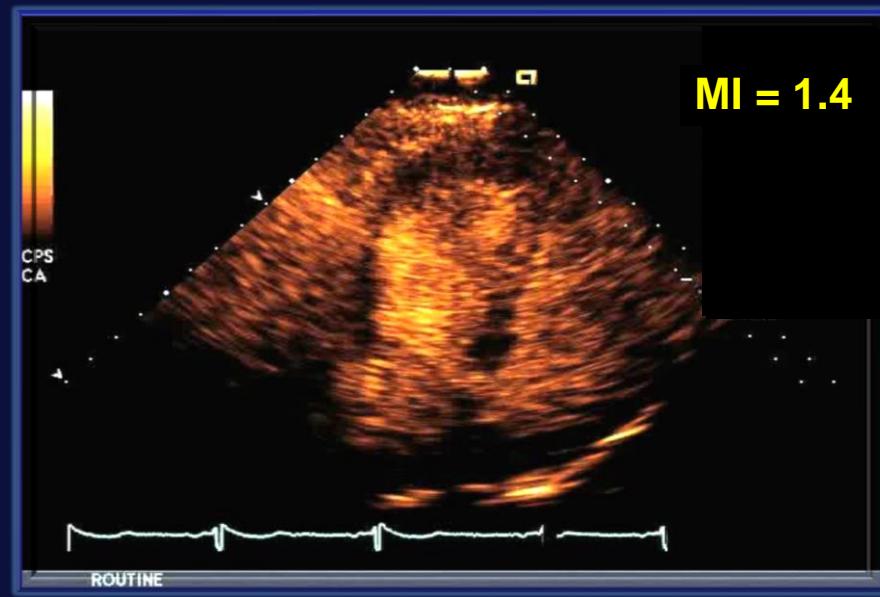
Impact of Mechanical Index

Mechanical Index

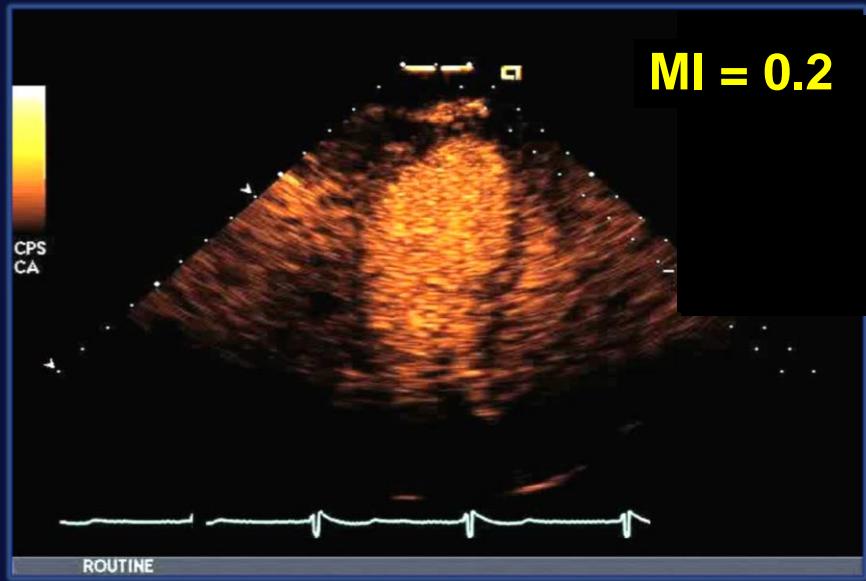
- Measure of output acoustic power
- High MI increases bubble destruction



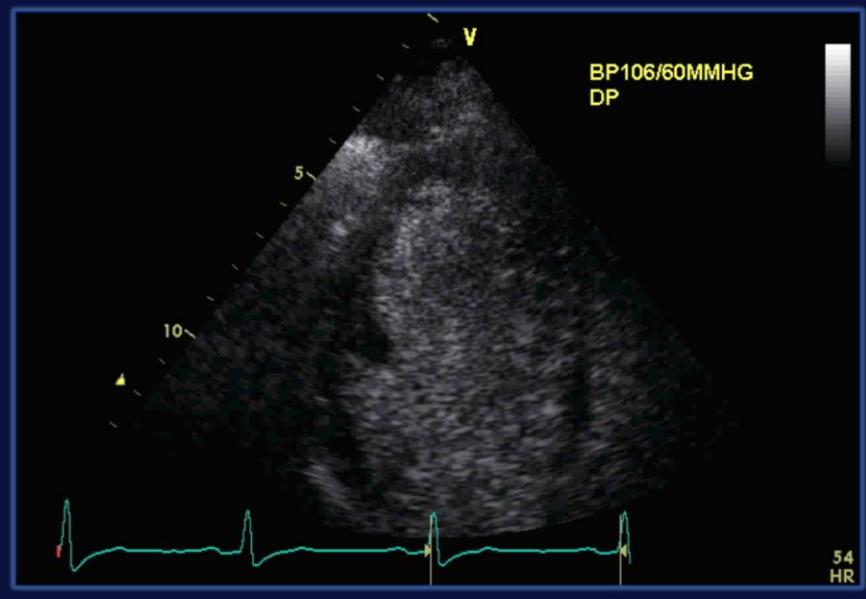
Suboptimal LV Opacification



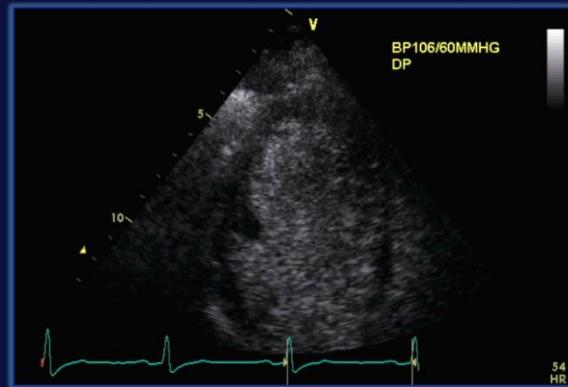
Optimal LV Opacification



Apical Dropout

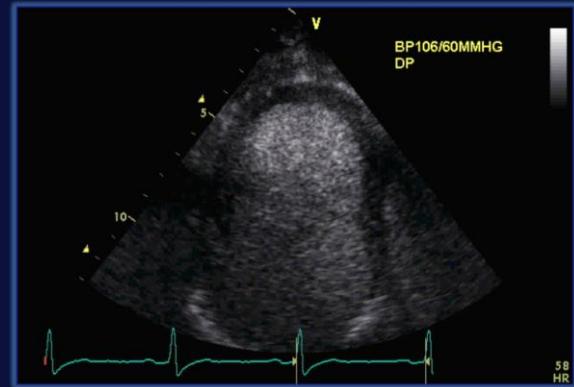


Apical Dropout



POTENTIAL CAUSES

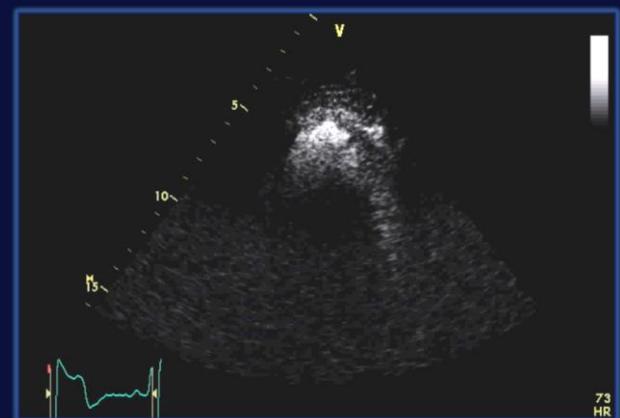
- System settings
(*focal zone misplacement*)
- Dosing and administration
(*low concentration*)



Attenuation

POTENTIAL CAUSES

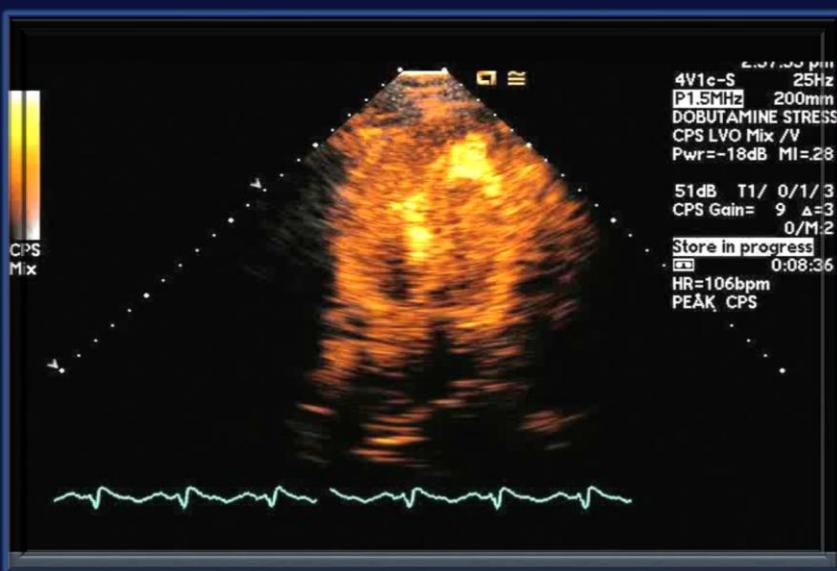
- Dosing
(*high concentration*)
- Administration
(*infusion rate too fast*)
- Clinician
(*obtain off-axis windows*)



Tincture of Time



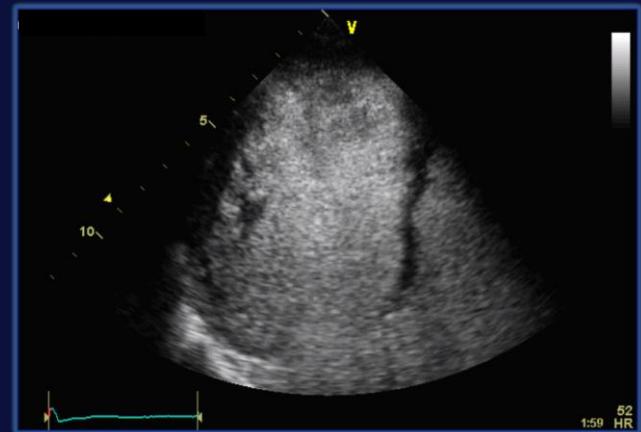
Burst Some Bubbles: Flash



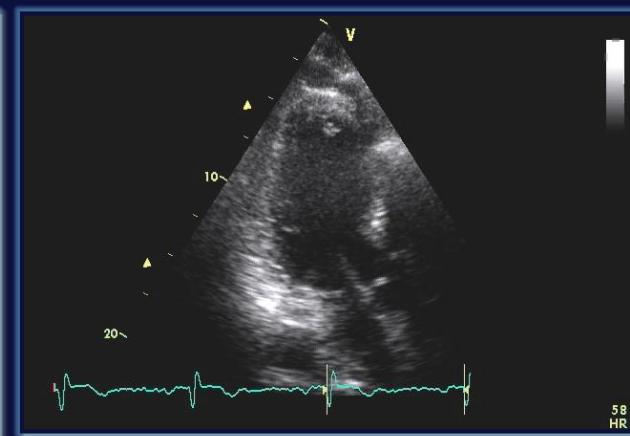
Swirling

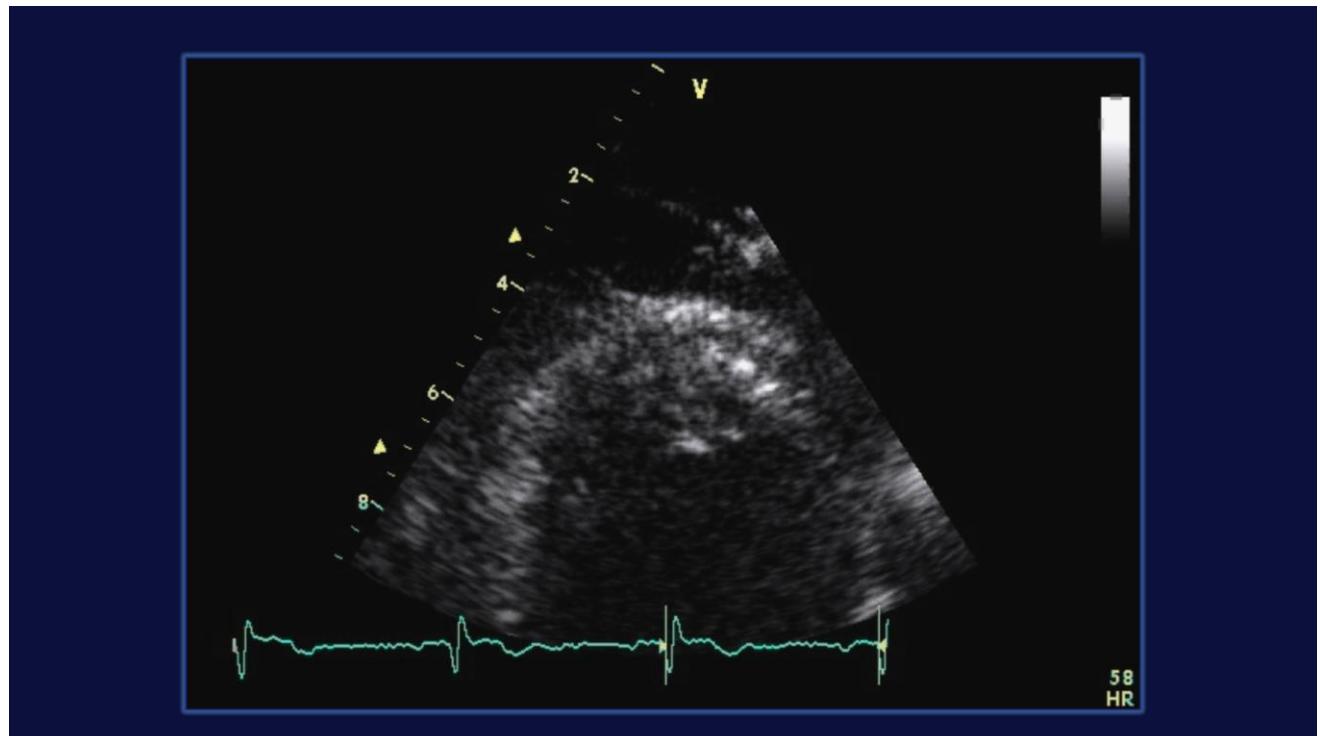
POTENTIAL CAUSES

- System settings
(high MI)
- Dosing
(low concentration)
- Administration
(low infusion rate)
- Poor LV function



Thrombus?

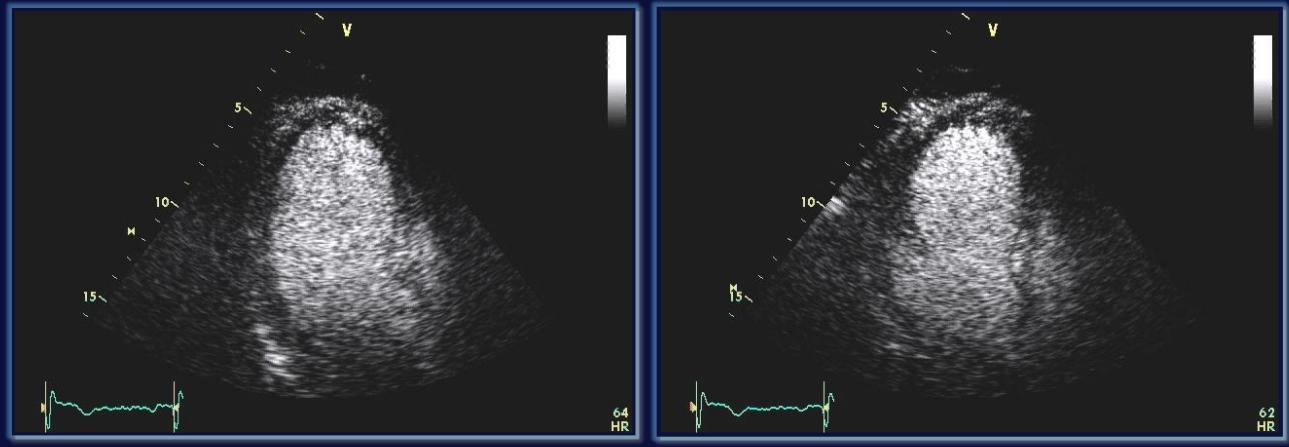




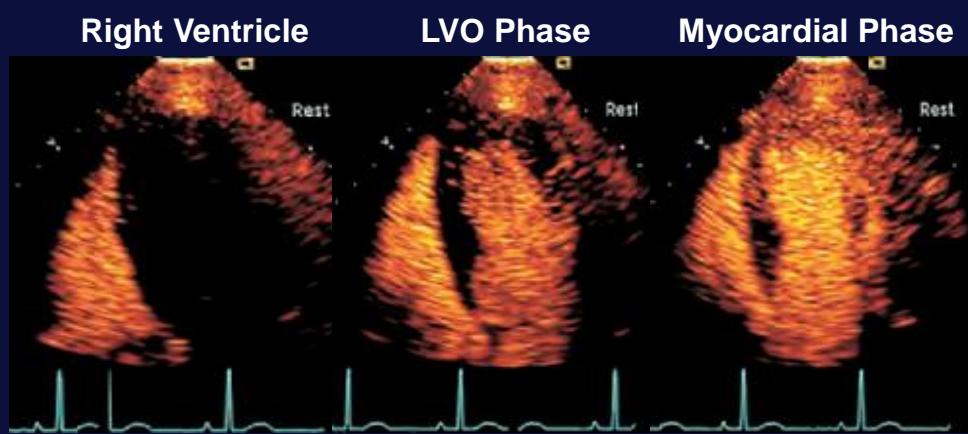
Did Contrast Help?



Instrument Set Up



Myocardial Contrast Echocardiography Perfusion



J Am Soc Echocardiogr 2008

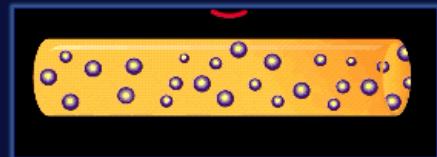
Myocardial Contrast Echocardiography Perfusion

Low MI, Nondestructive
Real Time



Continuous Imaging

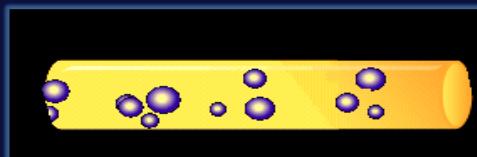
High MI, Destructive
Triggered



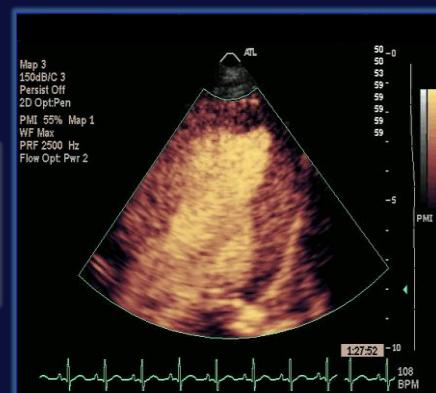
Intermittent Imaging

Myocardial Contrast Echocardiography Perfusion

Low MI, Nondestructive
Real Time

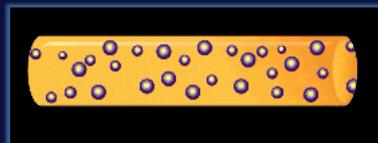


Continuous Imaging



Myocardial Contrast Echocardiography Perfusion

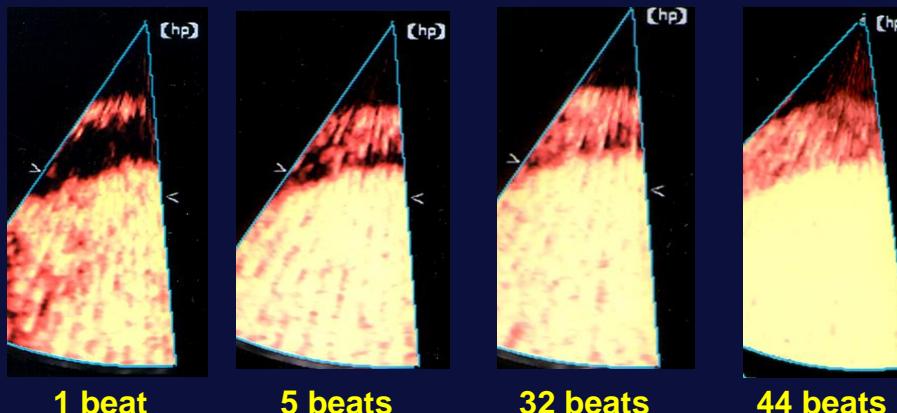
High MI, Destructive
Triggered



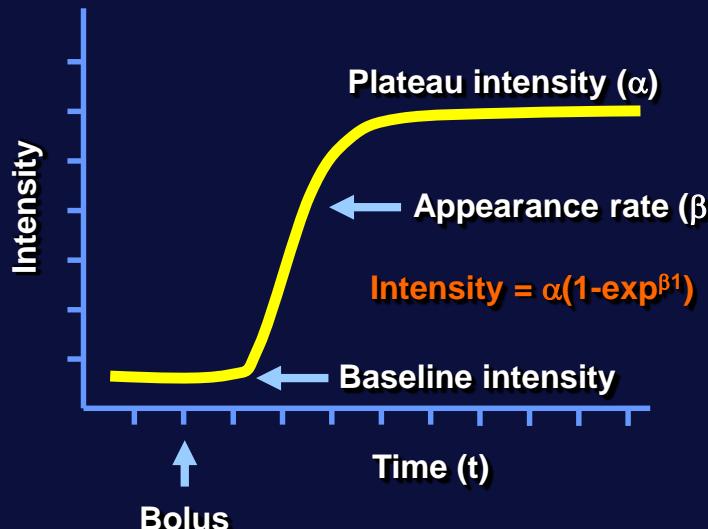
Intermittent Imaging



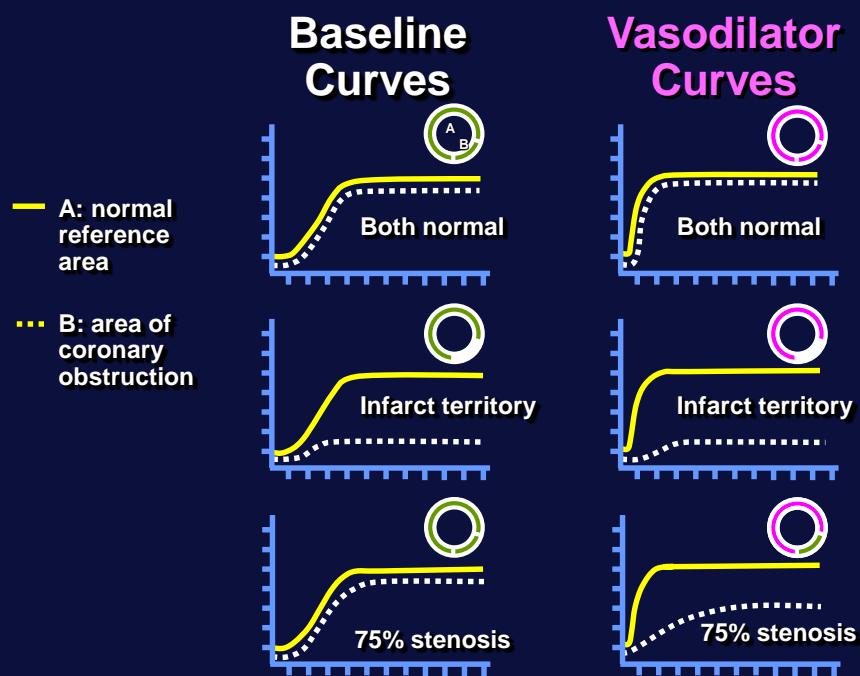
Triggering



Time Of Appearance Curve



Feigenbaum's Echocardiography 6th edition



Feigenbaum's Echocardiography 6th edition

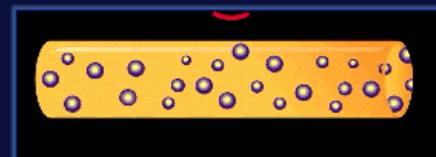
Myocardial Contrast Echocardiography Perfusion

Low MI, Nondestructive
Real Time



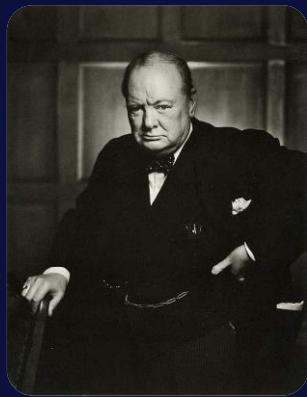
Continuous Imaging

High MI, Destructive
Triggered



Intermittent Imaging

Safety of Ultrasound Enhancing Agents



Sir Winston
Leonard Spencer
Churchill
(1874-1965)

"When I look back on all the worries I remember the story of the old man who said on his deathbed that he had a lot of trouble in his life, most of which never happened"

Safety: Contraindications

1. Suspected hypersensitivity to the microsphere components.

- Most serious reactions occur within 30 minutes of administration

**No 30 minute
monitoring period!**

True Incidence of Serious Adverse Events? **Mayo Clinic: 15 559 Doses**

- Any Adverse Reaction 0.6% (1 in 154)
 - Back pain n=75
 - Headache n=9
 - Urticaria n=17
- Urticaria/urticularial-like reaction 0.1% (1 in 915)
 - - Without Respiratory Symptoms n=12
 - - With Respiratory Symptoms n=5

Lester SJ et al J Am Soc Echocardiogr 2008;15:417

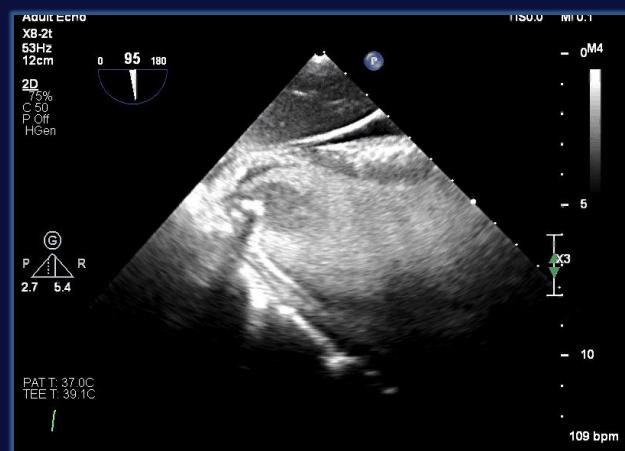
Ultrasound Contrast Anaphylactoid Reactions

CARPA

Complement Activation Related Pseudo Allergy

- Features similar IgE-mediated Type 1 reactions.
- Angioedema, bronchospasm, hypoxemia, hypotension, low back pain, and urticaria
- Can occur without prior exposure, decrease in severity with subsequent exposure, resolve spontaneously.

Contrast Echocardiography Tool Used to Build Excellence in ECHO



Take Home Points

- 1. The clinical utility of a bubble depends on its size, shell and type of gas**
- 2. *The backscattered signal radiating from a bubble that oscillates in a nonlinear fashion will contain a harmonic component.***

Take Home Points

- 3. Perfusion:**
 - Low MI, nondestructive, real time imaging
 - High MI, destruction, triggered imaging
- 4. The only contraindications is a hypersensitivity to the microsphere components**



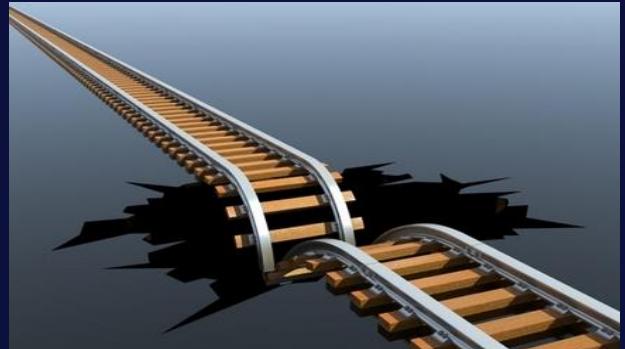


Contrast Echocardiography

Positive Impact : Makes a Difference



Avoid the Pitfalls: Big 5



Innovation



Workflow

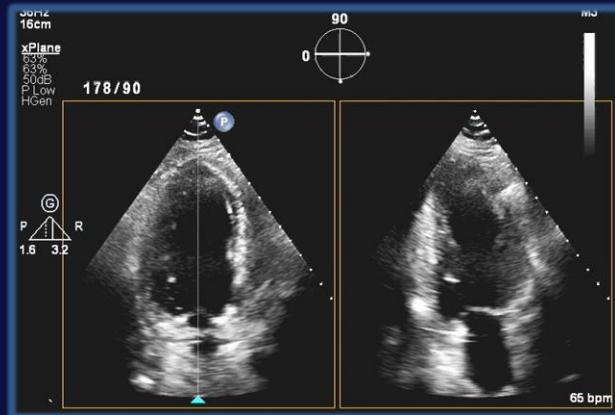


For any innovation in echocardiography to be widely adopted it must be equaled or paralleled by an innovation in workflow

Pitfall #2

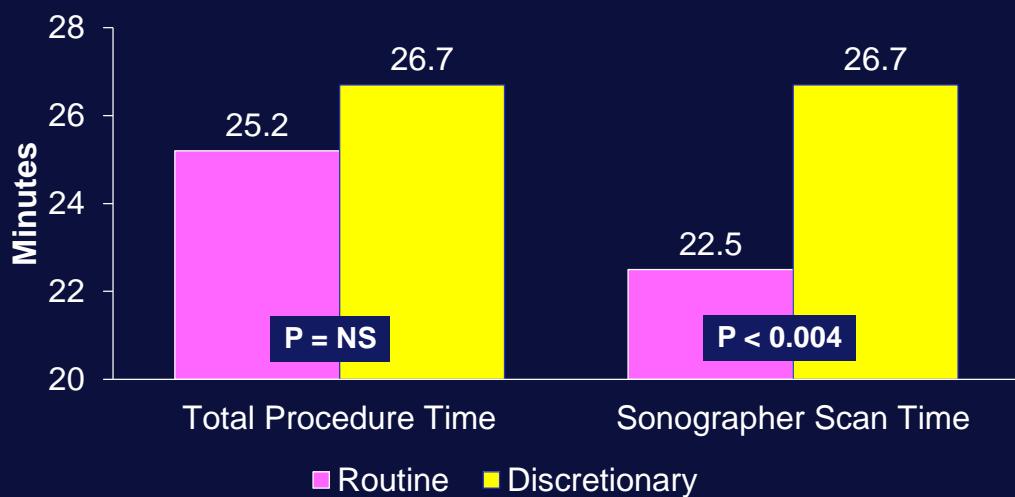
Imaging Protocol (a) : Workflow Efficiency

The “60 Second Echo”



Pitfall #2

Impact of the “60 second Echo”



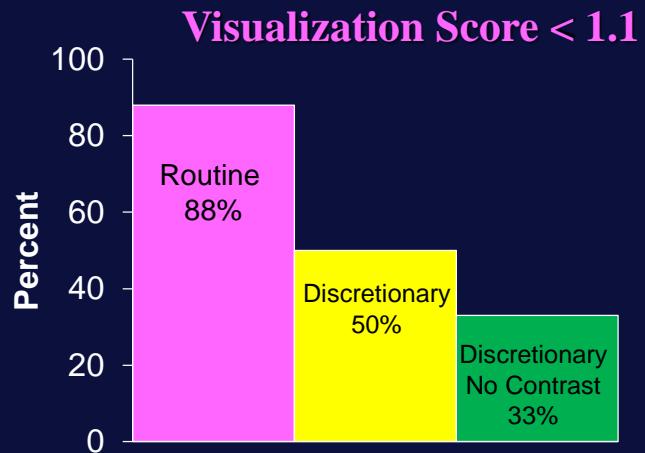
Lester SJ et al. J Am Soc Echocardiogr 2006 Jul; 19(7):919-23

Pitfall #3

We Don't Use Enough Contrast

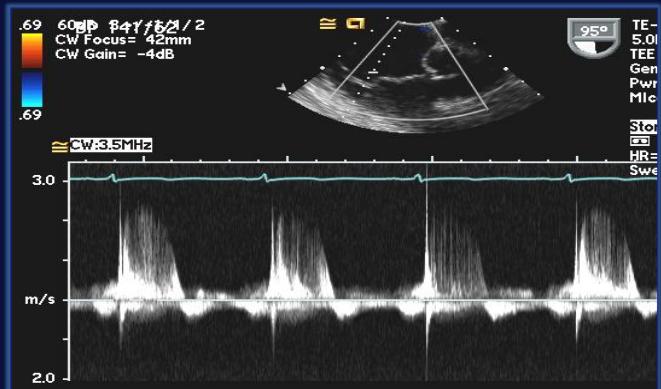
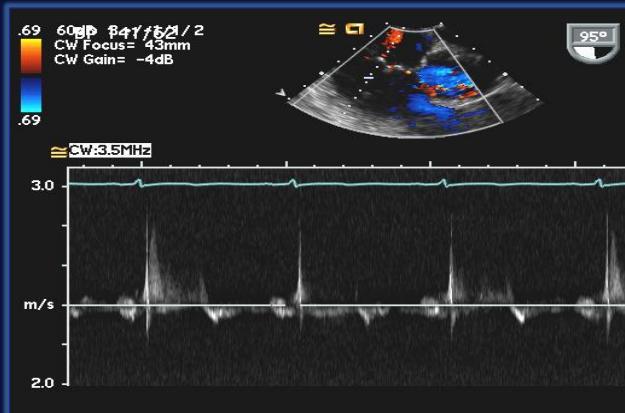
Visualization

- 1= Excellent or adequate full endocardial visualization**
- 2= Incomplete endocardial visualization**
- 3= only epicardium visualized**
- 4= segment not visualized**



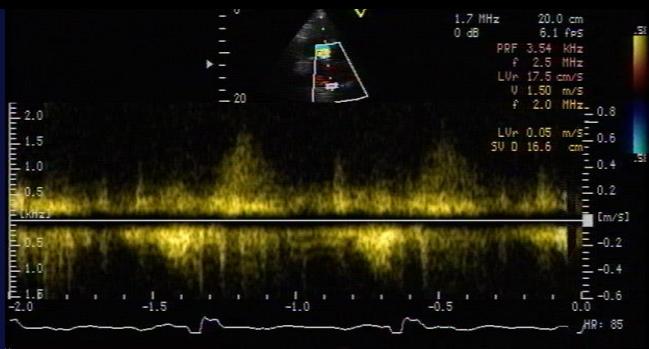
Lester SJ et al. J Am Soc Echocardiogr 2006 Jul; 19(7):919-23

TEE TR: Contrast

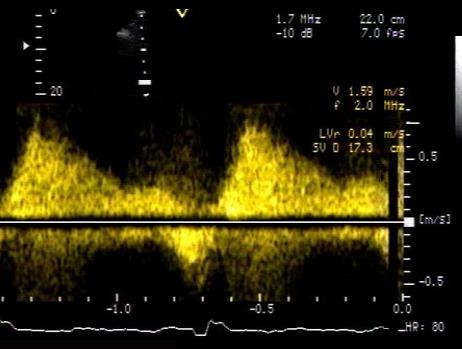


PULMONARY VEIN FLOW

Without Contrast



With Contrast



Contrast Echocardiography Avoid The Pitfalls



1. Contraindications (safety)
2. Protocol Development
(The 60 second Echo)
3. Use It
4. Spectral Doppler
5. Instrument Settings